ARS National Research Program

NRP NO. 20440 C nimal diseases—
infectious, non-inf

October 1976
U.S. Department of Agriculture
Agriculture Research Service

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NRP NO. 20440 Control of sheep and other animal diseases—infectious, non-infectious, and parasitic

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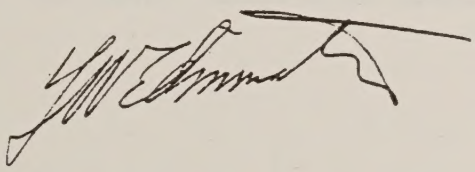
PREFACE

This document is one of the ARS National Research Programs (ARS-NRP's) or one of the ARS Special Research Programs (ARS-SRP's). These programs provide the basic plans for research in the Agricultural Research Service. The ARS-NRP's and the ARS-SRP's are a part of the ARS Management and Planning System (MAPS). The plans identify national research objectives, describe methods for achieving these objectives, and provide the accounting and reporting system by which these program areas are planned and managed.

Each of the ARS National Research Programs and Special Research Programs outlines a 10-year plan that describes current technology and new technology expected in the 10-year period. The plan includes approaches to research and benefits expected to result from new technology. The Special Research Programs facilitate research planning and management in those exceptional circumstances where special funds are involved or a different kind of research management is needed. They provide the same general type of information as the ARS-NRP's. Both types of research programs were prepared by the National Program Staff with the cooperation of Regional Staffs and Line Managers, Technical Advisors, Research Leaders, and other scientists.

These research plans will be used for a variety of purposes. They serve to link ARS research projects to major program areas involving several agencies within the USDA program structure. ARS-NRP's and ARS-SRP's identify important national problems and describe plans for achieving technological objectives. They provide justifications for current research activities and the basis for funds for future research. They serve as the basis for program reports and for the Agency's accounting system. They also improve the communication between scientists and management, between research managers and staff scientists, between ARS and other research organizations, and between USDA and other departments, the private sector, and Congress.

These documents are dynamic statements of ARS research plans and, as new knowledge is developed, they will be continually updated to reflect changes in objectives and research approaches.



ARS-NRP No: 20440
USDA Program: 22-678

CONTROL OF SHEEP AND OTHER ANIMAL DISEASES

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NRP 20480 Control of Insects Affecting Livestock

ARS-NRP No: 20440
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CONTROL OF SHEEP AND OTHER ANIMAL DISEASES

I INTRODUCTION

Diseases and parasites of sheep and other animals constitute major causes of loss to farmers, ranchers, and other users of several animal species, including those intended for pleasure. Feasible elimination of these deterrents to animal health depends upon development of data derived from sound basic and applied research and effective application of efforts to control them.

The sheep industry of this country provides valuable resources of high quality protein as food and desirable fiber for a number of purposes. As an industry, it is not as flourishing as those of other species in U.S. animal agriculture; namely, poultry, cattle, swine, and dairy. It should be realized, however, that the potential for development of the sheep industry in this country is very favorable.

The U.S. horse industry consists of animals used to a very minor extent for draft, but one that has had, during recent years, noticeable increases in numbers used for racing, pleasure, and several other types of work, including ranching. The contributions that these animal species can make to food production, recreation, and utilization of renewable natural resources are of both economic and humanitarian significance.

II ARS NATIONAL RESEARCH PROGRAM SUMMARY

A Current Technology. Although there is a great need for new technology by the different animal industries represented in this NRP, there are available new techniques for the detection, treatment, and control of several infectious and parasitic diseases and toxic conditions; a few are--respiratory diseases and bluetongue of sheep, encephalitides, infectious anemia, and piroplasmosis, and gastrointestinal parasites affecting both species.

Progressive pneumonia of sheep is a slow viral disease that has long been recognized in the Rocky Mountain Region of the U.S. and has spread to the Midwest. The disease usually results in death of affected animals at periods varying from six months to three years. It can be easily confused with similar diseases reported from several foreign countries and must be differentiated from them. An effective experimental diagnostic test for this disease has been recently developed. It is being used in the early stages of efforts to determine the incidence of the disease in this country.

The diagnosis and confirmation of bluetongue (BT) have been greatly improved. Also, time required for these procedures has been reduced by the use of the agar gel precipitin (AGP) test and tissue cell culture techniques developed by ARS. The AGP test is now being used by virtually everyone conducting epidemiological research on the disease in this country, and materials and procedures for its use have been requested by about a dozen different foreign countries. The tissue cell culture isolation system for confirmation of diagnosis of BT and epizootic hemorrhagic disease is being used by the Animal and Plant Health Inspection Service Diagnostic Laboratory and many state diagnostic laboratories. It provides a cheaper and faster confirmation of the diagnostic test when compared to previously conventional sheep and egg inoculation procedures.

Results of research showing interference of detectable immunity derived from vaccination for eastern, western, and Venezuelan encephalitis have been responsible for current recommendations that vaccines for these diseases be administered simultaneously. A killed vaccine has been developed and shown effective against the three encephalitides-causing viruses and is currently being marketed by commercial interests.

Only recently an effective blood test for diagnosing equine infectious anemia (EIA--swamp fever) was developed by other researchers. ARS scientists have developed an improved antigen for use in diagnostic testing procedures. The antigen is produced from infected cell cultures and results in a more standardized and economical reagent enhancing the usefulness of the test.

Equine piroplasmosis (EP) is caused by parasites that attack red blood cells and is transmitted from horse-to-horse by ticks. EP is clinically indistinguishable from EIA. ARS scientists have developed a complement-fixation test that is now used as the official diagnostic test for EP. The use of this test makes it possible to distinguish between the two diseases.

Although there is significant expense relating to materials and increased labor required, the use of chemical agents is the most reliable and practical means of combating gastrointestinal parasites.

B Visualized Technology. Continuous and possible expansion of research along the lines described in this NRP will result in an increased and more profitable supply of food, fiber, recreational resources, and feed utilization. Improvements in genetics and other factors, including nutrition, disease management, etc., are expected to result in significant increases in sheep production and utilization. Trends within the horse industry in this country indicate an increase that will be accentuated by the application of new technologies as they are developed by research.

Several diseases of these animal species are also transmissible to and affect humans. Examples are: Encephalitides affecting horses, leptospirosis, brucellosis, anthrax, influenza, tetanus, tuberculosis, and others.

It is not practical for this purpose to elaborate on all technologies having a bearing on each of the disease entities described in this NRP. Only a few of the more significant diseases of sheep and horses are elaborated on in this summary.

Respiratory diseases of sheep--Improved and standardized diagnostic and testing procedures can lead to more accurate definition of the incidence and severity of this condition in sheep. More sophisticated information about the causative agent of the disease itself can result in effective immunization products and procedures.

Bluetongue--New and improved diagnostic tests and isolation techniques for bluetongue ruminants will enhance ability to deferentiate this from other diseases causing similar signs in animals, as well as contribute to the development of more effective, practical immunizing products and procedures. Advances in livestock insect control (NRP 20480) and better definition of genetics of bluetongue virus resistance and susceptibility in insects will contribute greatly to the control of bluetongue.

Equine encephalomyelitides--Additional information on the various virus causative agents and insect transmission of these diseases will lead to better disease control through the use of vaccines and insect control measures.

Equine infectious anemia--Better understanding of the mechanism by which the virus persists in the presence of antibody in infected horses will greatly increase the speed with which effective immunization and control measures can be designed.

Piroplasmosis--Better understanding of the blood parasites causing this disease and mechanisms of infection, including immunity, and better definition of insect vectors will greatly enhance programs for the accurate diagnosis of the disease and safe procedures for increased traffic of horses.

Gastrointestinal parasites--Innovative research approaches can result in less expensive, yet effective, methods for eliminating gastrointestinal parasites from animals and immunizing and other biological methods for control.

C Consequences of Combined Visualized Technology. When the visualized technologies are developed and applied, several changes can be expected in animal agriculture. The understanding necessary for detection, control, and prevention of diseases of numerous animal species will result in their being reduced considerably. This reduction will have unpredictable impacts on regulatory programs, both Federal and State. The changes will result in different practices for managing those factors that affect animal health as it regards movement of animals, introduction of animals into existing herds and flocks, quarantine procedures, and economies related to animal agriculture. This is of particular significance considering this country's position as a producer and distributor of the most complete protein for human dietary purposes.

It can be expected that changes will necessarily be made regarding legal, economic, and social patterns, as well as those related specifically to agriculture.

D Total Potential Benefits. Total potential benefits from the animal health-related subjects dealt with in this NRP cannot be estimated with reasonable accuracy. It is obvious, however, that reduction of occurrence of the conditions described will materially benefit domestic livestock, livestock producers, and consumers by increasing production capacity, reducing cost of production per unit, and improving product quality. In addition, some public health concerns related to animals will be alleviated. Many of these things do not lend themselves to value quantitation.

Summary Total Potential Benefits

	Estimated Annual Losses $ Million	Percent Reduction	Total Annual Potential Benefits $ Million
T01 - Improve methods to minimize losses from disease			
Sheep			
Respiratory diseases	20.0	50	10.0
Roundworms, liver flukes, and tapeworms	97.7	50	71.3*
Bluetongue	7.1	30	2.13
Horses			
Equine encephalomyelitides**			
Equine infectious anemia	145.8	50	72.9
Helminths	50.0	50	25.0
Piroplasmosis**			
Other Animals			
Mink	5.0		
Rabbits	4.7		

*1978 Projection
**Continually recognized conditions for which no bases have been developed for estimation of losses caused by them.

Estimated annual losses and potential benefits shown on this table are not inclusive for all aspects of the diseases affecting sheep, horses, and other animals. For this reason, they have not been totaled. Sections have been left blank for which reasonably accurate information is not available.

E Total Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	17.5	$2,243,847	29.6
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		10±

NOTE: The expanded support level reflected in this National Research Program represents Staffs' views as to the additional level of staffing that can be effectively used in meeting the long-term visualized objectives for this program. These do not reflect commitments on the part of the Agency.

III TECHNOLOGICAL OBJECTIVE

III.I Improve methods to minimize losses from disease.
(See NRP 20420, Control of Cattle Diseases; NRP 20380, Production of Sheep and Other Animals; 20450, Control of Poultry Diseases; NRP 20470, Toxicology and Metabolism of Agricultural Chemicals and Poisonous Plants; NRP 20480, Control of Insects Affecting Livestock).

Several diseases of sheep that cause problems to the industry, but for which only varying amounts of research support are expended by ARS, usually for extramural research at other institutions, include scours, foot rot, enzootic abortion, vibrionic abortion, caseous lympadenitis, epididymitis, stiff lamb disease, and pregnancy toxemia.

Coccidiosis is a serious disease in sheep in the Mountain States. It is a particular problem in feedlot lambs and lambs that are put on pasture. It causes significant mortality and morbidity. It has been estimated that about 5 percent of the 1/2 million head annual lamb crop are affected and show clinical signs of coccidiosis and that about 10 percent of the affected lambs die. The annual loss attributed to death losses alone in one state--Colorado--is estimated to be about $125,000. Morbidity losses are greater, but not readily calculable. It has also been estimated that losses due to this condition in the 10 midwestern and western sheep-producing states are in excess of $13 million annually.

The biological aspects of coccidia affecting sheep are very similar to those affecting cattle and are described in more detail in NRP 20420.

Sheep

1.1 Respiratory Diseases of Sheep

A Current Technology. Although there are several respiratory diseases affecting sheep, to varying degrees, in this country, the ARS research effort is being concentrated on progressive pneumonia, which is described in detail in this section of the NRP.

Progressive pneumonia of sheep is a slow viral disease endemic in the sheep population of the Rocky Mountain Region of the U.S., with recent spread to the Midwest. It is a chronic respiratory ailment with an insidious onset, followed by slow, relentless progression to death. Horizontal transmission has been known for many years and a recent study has indicated the possibility of vertical transmission. Sheep are 3 years of age or older before signs of disease are seen; fatalities result from 6 months to 3 years later. The disease is caused by a virus with certain apparent physical and chemical properties of the oncornaviruses. The cardinal physio-anatomic feature of the disease is impairment of pulmonary function by massive numbers of lymphoid cells in the lungs. In the U.S., the disease is similar to or perhaps identical to respiratory diseases (maedi, zwoegersiekte, la bouhite, and Graff-Reinet) of sheep reported from many other countries. The causal

agent is related to the virus of meningoencephalitic disease called visna. Chronic progressive pneumonia has been confused with pulmonary adenomatosis (jaagsiekte) of sheep--a disease with insidious onset and slow conclusion, closely simulating progressive pneumonia. Prevalence of progressive pneumonia in the U.S. is not known, but has been reported as high as 90 percent in individual flocks in other countries.

Technological information gained during the past 10 years has been through the study of chronic progressive pneumonia and related diseases. Much of this information has yet to be confirmed with the disease or etiologic agent as they occur in the U.S. Extrapolation of results from studies with visna virus, a closely related virus, indicates a close relationship between the progressive pneumonia agent and oncornaviruses. The similarities include physical and chemical properties, reverse transcriptase activity, and ability to transform cells in culture. Studies of the transmissibility and pathogenicity of the disease, particularly zwoegersiekte in Holland, has added the most recent knowledge, indicating the relatedness of certain diseases of the respiratory system and central nervous system of sheep. Also, this and other investigations have shown the serologic response of sheep to infection; however, little is known of the value of serologic tests for diagnosis. Little is known about the factors involved in the genesis of the cardinal feature of lymphoid cell accumulation in the lungs.

B Visualized Technology. Develop and refine a serologic test for use as a diagnostic tool; by serologic, pathologic, and virologic studies, evaluate the prevalence of chronic progressive pneumonia and differentiate from other chronic pulmonary diseases of sheep in the U.S.; determine the pathogenesis of the lung lesions, including determinations of virus localization in tissues, morphologic observations of pulmonary changes, and studies of lymphocytic activity during the course of experimental and naturally occurring disease.

By a more complete understanding of the pathogenesis of chronic progressive pneumonia and of factors influencing the susceptibility of sheep to the disease, it is anticipated that a preventive program can significantly reduce the incidence of the disease, perhaps by as much as 75 percent. With adequate diagnostic and control procedures, it is conceivable that the disease could eventually be eliminated from the U.S.

C Research Approaches. 1. Develop and refine a diagnostic test for chronic progressive pneumonia: Determine methods most suitable for producing and standardizing viral antigen; utilize standardized antigen to determine the most applicable test for the diagnosis of chronic progressive pneumonia; refine the selected test to the highest degree of accuracy for the system involved.

2. Determine the incidence of chronic progressive penumonia and differentiate from other respiratory diseases of sheep: Examine sheep serum samples from slaughterhouses and from range and farm flocks for specific antibodies; isolate and identify viruses from the respiratory system of sheep; examine pulmonary tissues for morphologic changes.

3. Determine the pathogenesis of chronic progressive pneumonia: Determine susceptibility of sheep and laboratory animals to strains of virus; determine the distribution of virus in experimentally and naturally infected sheep by isolation and fluorescent antibody procedures; evaluate the transmission of virus by various routes; evaluate sequential anatomical changes in the lungs of experimentally infected sheep; determine the serologic response of experimentally infected sheep.

4. Develop techniques to evaluate the immunologic characteristics of the lungs of normal sheep and of sheep with chronic progressive pneumonia: Evaluate the cellular and humoral response occurring in the lungs of sheep after challenge with living and non-living antigens; evaluate the immunologic response in the lungs of sheep during the course of infection with the virus of chronic progressive pneumonia.

D Consequences of Visualized Technology. Assist in clarifying the complicated respiratory disease problem of sheep and in eventual control of the problem. Provide protein food to the consumer at less expense. Increase the income of sheepmen and help stimulate the sheep industry.

E Potential Benefits. Because of the voids in statistical information on chronic progressive pneumonia, many assumptions must be made. Assuming an infection rate of 2 percent and an average decrease of 1 year productivity, there would be an annual loss of replacement cost of 0.66 million head of sheep. This loss to the sheep industry approximates $20 million, most of which could be saved by adequate control and preventative measures.

This estimated loss would be greatly increased if, as anticipated, during the long incubation period, the progressive pneumonia virus predisposes younger sheep to other respiratory infections.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	2.0	$233,265	3.0
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		8

1.2 Roundworms, Liver Flukes, and Tapeworms of Sheep

A Current Technology. Losses to the sheep industry due to internal helminth parasites (worms) fall into four main categories: Mortality--or deaths of breeder stock and lambs produced for market; morbidity--represented by reduced yield of meat and wool, waste of feed and labor, interference with breeding and reproduction, reduced quality of animals (both breeder and production stock), and lowered resistance to infectious diseases; control costs--drugs for treatment and prevention and veterinary services; condemnations of carcasses and parts at abattoirs--of livers because of flukes and tapeworms.

In 1973, losses attributed to helminth parasites of sheep were $39.7 million or approximately 6 percent of the total value ($540.7 million for sheep and lambs; $120.5 million for wool) of sheep production for that year. The above loss figure does not include the cost of medication and care of parasite-affected animals, which is estimated to be an additional $24.4 million.

Losses attributed to internal helminth parasites are not distributed evenly throughout the country, but occur to a greater degree in the South, where a warm climate and moderate to high annual rainfall produce lush pastures. Concentration of sheep to utilize these pastures to the fullest extent to obtain greater productivity per land unit results in multiplication of problems of parasitism with increases in losses. In the West, sheep can be raised with fewer losses on undeveloped land, but fewer sheep can be produced per land unit. In the Southwest, particularly southwestern Texas, where the highest number of sheep are raised, the losses from helminths have been increasing in recent years. Even though total rainfall is low, the concentration of sheep in the better range lands of the valleys has resulted in these losses. Productivity of this land can be increased through irrigation and pasture improvement, but with concentrations of more animals, losses from internal parasitism increase.

Current control is effected largely through the use of chemotherapeutic agents. The use of these agents, usually as specific treatments, is the most reliable and practical available means of combating helminthic infections. Despite great progress in the last two decades, there is still a lack of chemical measures for controlling more than half of the injurious helminths of food animals. Specifically, in sheep, completely satisfactory treatments are not available against parasites such as hookworms, whipworms, capillarids, gullet worms, lungworms, filariae, liver flukes, and tapeworms. There are no available means for destroying infective eggs and larvae on pasture, the major sources of infection of grazing animals.

Present research results suggest promising new approaches toward preventing and reducing the depredations of helminth parasitism through a better understanding of host-parasite relationships, novel management practices minimizing exposure of livestock to infective stages of the parasites, and the great potential of immunological and other biological or nonchemical control measures.

Specifications: Direct losses from internal parasites--$39.7 million/year. Cost of medication and care of sick animals--$24.4 million/year. Losses of feed efficiency due to internal parasitism--$33.6 million/year.

B Visualized Technology. Reduce the annual losses from internal parasites of sheep through development of better pasture management systems to increase productivity of the land units while preventing parasitism; development and evaluation of more effective and less costly anthelmintic drugs and by experimental surveillance of such drugs to prevent losses resulting from the occurrence of drug-resistant strains of helminths; combinations of management and strategically timed treatments; use of biological means of control, including the development of effective vaccines.

The losses to be reduced include mortality, morbidity (reduced yields of meat and wool), drug costs and lowered digestibility of roughages.

Specifications: Direct losses from internal parasites--50% reduction in losses. Cost of medication and care of sick animals--50% reduction in losses. Loss of feed efficiency due to internal parasitism--50% reduction in losses.

C Research Approaches. Basic and applied research are required to determine biology and ecology of the various helminth parasites infecting sheep; effects of these parasites on sheep; methods of preventing infections; means of terminating acquired infections; and identification and classification of parasites encountered. Research includes a program in animal management, immunology, pathology, bioclimatic ecology, epizootiology, biochemistry, systematics, and parasitology.

Most of the research will be directed to three major approaches:

1. Increased resistance of sheep to infection by helminth parasites or to the effects of parasitism: What physiological factors are involved in resistance to parasitism? Can resistance be acquired through the use of nonpathogenic forms for immunization procedures? Can a vaccine be developed to protect against parasitism? What is the best way of purifying and characterizing helminth antigens? What purified antigens are related to immunological phenomena? Do nonprecipitating reagin-like antibodies activate tissue response in the host against helminths? What immunological properties are present in immune mucosal extract, and how does this inhibit the development of gastrointestinal worms? Are there specific immune globulins, localized or general, that can be related to antiparasite activity? What stages of parasites are affected by immune sera, and when is the most opportune time in the parasitic cycle to use such sera to immunize sheep? Why do grazing animals become susceptible to reinfection while experimental infections often result in a strong resistance to reinfection? What breeds of sheep are more resistant to the establishment of internal parasitic infection? What breeds of sheep are more resistant to the effects of internal parasitism? Are resistances hereditary and can they be increased through selection?

2. Prevention of infection of sheep: What management practices will circumvent infections by parasites, or what are the ways by which infections are acquired? Will early lambing or season of birth affect acquisition of parasites? To what extent are infections carried over from year-to-year by means of contaminated pastures? What are the bioclimatic limits of temperature, moisture, and light, operating singly or in combination, for the development and survival of the free-living stages of sheep helminths? Can clinical parasitism be predicted through bioclimatic records used in conjunction with current or long-range forecasts of weather conditions? What effect does surface structure of plants have on the migration of infective larvae? What are the effects of stress factors such as shipping, lambing, etc., on the susceptibility to helminthic disease? Can liver fluke infection be prevented or controlled by biological control based on trematode antagonism with the snail intermediate host? Under in vitro conditions, what are the specific nutritional requirements for the maintenance, growth, and maturation of the various stages of helminths? How and in what quantity are proteins and other substances metabolized by parasites grown in vitro or in vivo conditions? What changes in the concentration of carbon dioxide and ruminal acids and in pH affect the exsheathment and establishment of abomasal helminths? What helminths are prevalent on irrigated pastures of the Southwest, and how and to what extent do these helminths affect sheep going on to irrigated pastures from range grazing? What is the relationship of helminthic infection to the incidence and severity of protozoan, bacterial or viral diseases? How does the chemical physiology of the parasite differ from the host as related to the eventual development of antimetabolites to combat the helminths? What are the normal values of serum constituents in sheep as related to management, age, and sex? What changes in serum constituents, including minerals and vitamins A, C, and B_{12} occur in infected sheep?

3. More effective anthelmintics and the strategic use of them: What new anthelmintics are most effective? At what time of the year do anthelmintics prove to be most effective? How important is the build-up of resistance by the parasites to an anthelmintic, and what are the factors, genetic and/or physiologic, involved in this resistance? What regimens are best for treating with anthelmintics? What is the fate of various anthelmintics in sheep, including absorption, mode of action, detoxication, and excretion? What chemicals can be used as ovicides or larvicides that are safe for the animals and do not interfere with the normal growth of grasses and other forages? What effect does the use of chemicals have on the development and retention of immunity by sheep against helminths? How does the chemical physiology of the parasite differ from the host as related to the eventual development of antimetabolites to combat the helminths? How effective is the alternation of chemicals in treatment regimens, and can two or more anthelmintics be combined to enhance their efficacy? What changes occur in the physiology of parasitic organisms under in vitro conditions, including enzymatic activity and respiration, after drugs or metabolites of drugs have been added to the parasite culture media? Is the effectiveness of anthelmintics affected by differences in the physiology of individual animals? What adverse effects do anthelmintic drugs have on reproduction and other physiological functions of sheep?

D Consequences of Visualized Technology. Reduce losses to sheep producers from sheep mortality and morbidity due to helminths. Reduce farm costs for chemotherapy. Increase the number of meat animals and pounds of wool for market. Improve the utilization of feed. Acquire information that will help in helminth problems of cattle production. Acquire knowledge that will help in preventing and/or treating helminth infections of humans. The development of an effective larvicide against the intermediate stages of such helminths found in humans. Reduce cost of lamb and mutton to consumers.

E Potential Benefits. The annual farm value of sheep and wool production was $473 million in 1973. The projected needs for lamb and mutton in 1985 are for a 58 percent increase that would require that the 1973 population of lambs be increased from 12 to 19 million.

Reduce direct losses from internal parasites: Current losses are estimated at $39.7 million annually. Comparative losses in 1985 would be 39.7 x 1.58 or $62.7 million. The cost of sustaining the technology is estimated at $4 million. Therefore, reducing the loss by half will provide $62.7 million x 1/2 - $4 million = $27.4 million potential annual benefit.

Reduce the cost of medication and care of sick animals: Current losses are estimated at $24.4 million annually. Losses in 1985 are estimated to be $24.4 x 1.58 or $38.6 million. With a 50 percent loss reduction and a sustaining cost of $2 million, there would be a $17.3 million potential annual benefit.

Decrease losses of feed efficiency due to internal parasitism: Feed costs due to parasitism are an estimated $33.6 million in 1973. Losses by 1985 would be 33.6 x 1.58 = $53.1 million. A 50 percent reduction in loss--$8 million for implementing the technology--would result in a potential annual saving of $18.6 million.

Total potential benefits quantitated: $71.3 million annually.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	1.7	$381,282	2.7
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		7

1.3 Bluetongue (BT)

A Current Technology. Bluetongue is one of the emerging diseases of livestock. Until recently, it was considered an obscure condition of sheep in Africa that caused low mortality and was only of academic interest to most veterinary workers. With recent serious extensions of the disease to new areas and the knowledge that it infects cattle, BT has attracted worldwide attention and is now a major nontariff trade barrier to the exportation of U.S. livestock.

Bluetongue is a seasonal viral disease of sheep, cattle, and other ruminants that has a worldwide distribution and is transmitted by a biting gnat, Culicoides spp. (C. variipennis in the U.S.).

Bluetongue virus (BTV) was initially identified as a disease of sheep in South Africa during the 19th century. The virus was isolated and identified in the U.S. from sheep in 1952 and from cattle in 1959. Until 1967, BT was thought to be restricted to the 22 contiguous states west of the Mississippi River, where 87 percent of the Nation's 14.5 million sheep (estimated 1975) and 68 percent of the Nation's 131.8 million cattle (estimated 1975) are raised in the U.S. It is now recognized that the BT enzootic area is fluid; BTV has been isolated from ruminants in 23 states and antibody has been serologically confirmed in ruminants from 46 states.

The causative agent of BT is a virus that is morphologically classified as an orbivirus. Bluetongue is an extremely pleomorphic virus as reflected by the identification of at least 16 serotypes by the World Reference Center in South Africa. At least 4 serotypes have been demonstrated in the U.S. These serotypic differences caused by immunologic or antigenic mutation are manifested by a broad range of virulence for the ruminant hosts as exhibited by mild to severe clinical illness.

A diagnosis of BT disease in ruminants is initially made from clinical signs, which are similar to those seen in foot-and-mouth disease, vesicular stomatitis, rinderpest, malignant catarrhal fever, infectious bovine rhinotracheitis and bovine virus diarrhea. A confirmed diagnosis of BT must be made in the laboratory by isolating and identifying the virus or by demonstrating specific serum antibody.

All viruses require living cells in which to replicate. Bluetongue virus has been traditionally and most consistently isolated by inoculating suspected tissue or blood samples into susceptible sheep or embryonating chicken eggs. Improved cell culture techniques and cell lines (VERO and BHK-21) have recently been demonstrated to be an economical, efficient, and sensitive alternative to sheep and chicken embryos for virus isolation. Laboratory animals such as suckling mice have not proved as satisfactory as other living systems for viral replication. Bluetongue virus is identified after isolation by using immunofluorescence techniques. Other more cumbersome identification techniques, such as complement-fixation and neutralization

tests are used, but are more applicable for experimental use. Complement-fixation tests are used more commonly for the identification and quantitation of specific antibodies in the serum of infected animals. Serum neutralization or plaque reduction neutralization tests are used for serotyping of the numerous antigenic variants of BTV. Electron microscopy can be used to demonstrate the presence and location of virus particles in cells and tissues of infected animals. Although this instrument will not reveal the identity of a virus, the electron microscope is used extensively in experimental studies on animals infected with known BTV.

Antibody to BTV in the sera of infected animals is identified and quantified by the modified direct complement-fixation (MDCF) test that is used as the standard test for international movement of sheep and cattle. A more sensitive test that is gaining worldwide acceptance for BTV field surveys is the agar gel precipitation (AGP) test. A passive hemagglutination-inhibition test was recently described for detection of BT antibody, but the test has not yet received wide recognition.

The control of BT requires a multifaceted approach since the epizootiology involves a host (sheep, cattle, wild ruminants), a vector (Culicoides spp.), and a virus. Vaccination of susceptible animals has been used to protect cattle and sheep for more than 70 years. Active immunization is currently practiced and involves the use of virus attenuated in embryonating chicken eggs or in cell cultures. Although polyvalent, avianized vaccines are used in Africa, these products are not used in the U.S. because the vaccine virus can be transmitted by insects from vaccinated to nonvaccinated animals with reversion of the virus to a more virulent form. A bovine kidney cell culture-adapted, monovalent vaccine is currently approved in the U.S. for use in sheep. In 1974, 609,000 doses of this vaccine were produced. It is estimated that 90 percent of the vaccine is used in Indian reservation flocks, in NM, AZ, and UT. Vaccine is used by livestock producers in only 4.2 percent of the Nation's sheep. Outbreaks of BT in individual flocks can be arrested within 14 days by vaccinating the sheep in a flock. In large flocks, the cost would run about 25 cents per head. This attenuated vaccine is inadequate due to the possible reversion of the virus to virulence and to the multiplicity of viral serotypes. Very little cross-immunity occurs among the serotypes with vaccination or infection. Work on an effective polyvalent, killed virus vaccine is only in the preliminary stages.

Bluetongue eradication is not realistic at this time because of the large enzootic area involved. The absence of a reliable, practical diagnostic test to identify infected livestock and other factors, such as the virus reservoir, are also important and will be discussed later.

One potential control measure for BT involves control of the vector. Culicoides gnats mature in the mud of pools of standing water that are contaminated with animal wastes or human sewage effluent. Ecologically compatible vector control involves proper drainage and repair of faulty sewage systems to destroy the breeding sites.

A revolutionary viral control method has been suggested by recent research that has demonstrated genetic control of BTV resistance and susceptibility to oral infection in C. variipennis. These traits segregate in only 1 to 2 generations, and it is possible to produce populations of gnats that are 100 percent transmitters or nontransmitters of BTV. It is theoretically possible to control BT disease without destroying the insect and disrupting the ecology of an area. The resistance of a population of C. variipennis to oral infections with BTV in a problem area may be increased by the release of viable, competitive, virus-resistant gnats. This biological, nonchemical control could be practical and nondestructive to the environment.

Scant information exists on the importance of other arthropods in the epizootiology of BTV. Melophagus ovinus, a wingless fly, has been shown to mechanically transmit BTV among sheep. Blood-sucking insects have not been sufficiently studied; however, Umatilla virus, an orbivirus related to BTV has been isolated from mosquitoes.

Epizootic hemorrhagic disease was initially identified as a lethal condition of deer in the U.S. and is caused by an orbivirus related to BTV. Although sheep are unaffected by epizootic hemorrhagic disease virus (EHDV), cattle can become severely ill after infection with a clinical syndrome that resembles BT. A diagnosis of EHD in cattle can only be made by viral isolation in embryonating chicken eggs, cell cultures, or suckling mice, and identification of the antigen by immunofluorescence. Initial serotyping efforts using the plaque reduction neutralization technique suggest that multiple EHDV serotypes occur.

Epizootic hemorrhagic disease is primarily a disease of deer. The extent of EHDV activity in the U.S. and the degree of cattle involvement are not known. C. variipennis is probably a vector, and insect control is the only measure available for EHD control.

Nearly 400 arthropod-borne viruses (arboviruses) have been identified in the world. Many occur in the U.S. and, although the disease potential of most is unknown, some may prove to be pathogenic for ruminants; e.g., Umatilla.

Diagnostic techniques for Umatilla and other arboviruses will be developed when needed for comparative studies with BTV and EHDV or when these agents are recognized as livestock pathogens.

The incidence of BT varies widely in the U.S. Most BT outbreaks in sheep have been reported in 7 states (CA, CO, AZ, UT, ID, NM, and TX), where 49 percent of the Nation's sheep, valued at $223,886,000, (estimated 1975) are raised. Bluetongue is most severe in lambs in which morbidity may approach 100 percent and is less severe in older sheep--morbidity 15 percent. Mortality in sheep can vary from 0 to 50 percent, recorded in lambs during an Idaho outbreak. The economic losses must be measured in terms of weight loss, poor rates of gain, wasted feed, damage to the fleece, expenses of veterinary services, and death. Most experts believe that sheep are the indicators of BTV activity and that cattle are the reservoirs or sources of infection.

Bluetongue in sheep is clinically manifested by a high fever (106° F), leukopenia, hyperemia of oral mucosa, and salivation. As the syndrome progresses, edema of the tongue, lips, face, and ears, hyperemia, petechial hemorrhages, and eventually ulceration and necrosis of the mucous membranes are observed. Coronitis, muscular degeneration, emaciation, dropping of the fleece, and death from secondary bacterial pneumonia occur.

In general, sheep experience only a short duration viremia during which time C. variipennis can become infected and transmit BTV to susceptible animals. Sheep that recover from BT develop a solid immunity to the homologous (infecting) serotype, but only a partial to minimal degree of protection is developed against heterologous serotypes.

Sheep are the most sensitive domestic animal hosts for demonstrating the presence of BTV. For this reason, sheep have been used for experimental work and, in Canada, sheep have been inoculated with blood and semen to certify cattle and semen for exportation.

It is now obvious that cattle may be the most important host of BTV in which a complex virus-host relationship develops that makes cattle an inapparent reservoir for virus, perhaps for life. Clinical illness is often not recognized in cattle and this has created a serious obstacle to the export of purebred cattle and semen to sheep-producing countries that believe their sheep industry is in danger.

Clinical BT in cattle is similar to the disease in sheep. It is now recognized that there are other more insidious and dangerous aspects to the infection. It has been experimentally demonstrated that bovine fetuses infected in utero by bites of BTV-infected C. variipennis on their dams develop immunological tolerance and can become persistently BT viremic through birth and adulthood. Such animals appear clinically normal, may not develop detectable serum antibodies, may not circulate detectable BTV in the blood at all times and the virus can be transmitted to susceptible cattle or sheep by the feeding of C. variipennis. Studies have shown that activation of detectable viremia requires stimulation of the host by C. variipennis bites before the commonly used isolation techniques; e.g., inoculation of sheep, embryonating chicken eggs, or cell cultures can be used to detect the steady-state viremia. Without insect stimulation, BTV can only be isolated routinely from cattle by using a blood autograft or autoinoculation technique in sheep.

Recent field studies suggest the involvement of BTV in the weak calf syndrome and lend support to experimental studies on in utero infections and the virus carrier state. Bluetongue virus has been isolated with a parvovirus from neonatal or stillborn calves and their dams on ranches near Denver. Ranchers have experienced a 50 to 100 percent calf loss, heifers and cows do not conceive, or they abort or resorb their fetuses. Other calves are weak and deformed at birth or are stillborn. It is unclear whether the two viruses are working independently or synergistically to produce this syndrome.

It has been determined that BTV is excreted into the semen of bulls for up to 110 days after BTV-infection by C. variipennis. Preputial ulcers and BT viremia commonly occur in these bulls and preliminary studies suggest that the virus is excreted into the seminal fluid by the seminal vesicles.

Bluetongue virus, EHDV, and other orbiviruses are double-stranded ribonucleic acid (ds-RNA)-containing viruses. The name "orbivirus" reflects the large doughnut-shaped capsomeres seen on the surfaces of negatively stained virus particles. Pathogens of man and domestic animals have been identified in this group. Orbiviruses are relatively resistant to lipid solvents and sodium deoxycholate and highly sensitive to acid pH. Orbiviruses measure 65 to 80 nm in diameter and mature in the cytoplasm as unenveloped particles that can be visualized with nucleic acid or immunofluorescent stains as inclusion bodies. Orbiviruses are classified as a group on the basis of physicochemical parameters and the serologic relatedness as demonstrated by complement-fixation tests.

The BTV soluble antigens produced in infected cell cultures are used in the agar gel precipitin (AGP) test for the diagnosis of BT by detecting BT-specific antibody. The source of soluble antigen, relation to the virion, and chemical composition are unknown. Improved BT diagnosis could result from increasing the concentration, sensitivity, specificity, or reactivity of soluble antigens by physicochemical methods. The diagnosis of EHDV and other orbiviruses is enhanced by the use of soluble antigens for AGP tests. Soluble antigens may offer an effective control alternative to BTV vaccines. Studies are planned to determine the immunogenicity of soluble antigens for protecting animals.

Physicochemical methods can be used to concentrate and purify viruses. By increasing the antigenic mass of BTV, an effective, immunogenic, inactivated virus vaccine may be produced.

Animal viruses have been believed to have fragmented nucleic acid genomes. Recent studies indicate that BTV ds-RNA is linear and may be active in vitro. An understanding of points of natural fracture in a genome and demonstration of in vitro translation and transcription can lead to viral hybridization studies. These data will assist in understanding and even predicting the nature of antigenic variation or serotypic differences in orbiviruses and other virus groups.

By using physicochemical methods, the nature, avidity, and specificity of antigen-antibody complexing can be better understood.

A population of C. variipennis from Sonora, TX, was colonized in 1957 and has been the standard model for all BTV experimental studies with the vector. This population has a consistent BTV infection rate of approximately 30 percent with most serotypes of BTV. By genetic selection, lines of C. variipennis have been derived from the parent population that are 100 percent susceptible or 100 percent resistant to oral infection with BTV.

Recently, other populations of C. variipennis were colonized from areas where BT outbreaks have occurred. Our studies suggest that these populations are, in general, most susceptible to oral infection with the BTV strain isolated in the area of the outbreak from which the colony was derived. There is an obvious differential susceptibility of different populations of C. variipennis to different serotypes of BTV.

In addition to its importance as a vector of BTV, C. variipennis is a fierce biting pest of humans and livestock. Swarms of these flies will attack the ears and abdomens of livestock. This disrupts feeding and makes the animals nervous and causes a scabby dermatitis.

Very little is known about the ethology-ecology, physiology, and microbiology of C. variipennis. The scanty information available on the habitats of C. variipennis has been used in recommending control measures. Transovarial transmission of BTV has not been demonstrated and the effects of BTV infection on the fly are unknown.

B Visualized Technology. Facilitate and hasten the diagnosis of BT, EHD, and other arbovirus diseases and provide practical control measures for these diseases and the vector, C. variipennis by: Developing practical, new, and improving existing diagnostic tests and isolation techniques for BT of sheep, cattle, goats, and wild ruminants, for EHD of cattle and wild ruminants and for other arbovirus diseases of sheep, cattle, and goats, as necessary; developing and comparing more rapid and sensitive serotyping techniques for EHDV and BTV; developing methodology for the production of immunogenic, polyvalent, attenuated or inactivated virus vaccines for BTV that could be applicable for EHDV and other orbiviruses; developing high volume serological techniques to follow antibody formation after natural infection or vaccination with BTV; developing nonchemical control methods for C. variipennis that are nondisruptive to the environment; establishing the roles of other biting flies and blood-sucking insects (e.g., mosquitoes) in the transmission of BTV, EHDV, and other arboviruses of livestock; determing the geographic distribution of BT in the U.S. and estimating the numbers of cattle, sheep, and goats threatened by, susceptible to, immune to, or infected with BTV.

Investigate the pathogenesis of BTV in cattle and sheep by: Determining the mechanism by which blood autograft permits the isolation of BTV strains from cattle that are of low virulence for sheep; examining the effects of C. variipennis-transmitted BTV on bovine fetuses and adults; determining the effects of BTV in semen on inseminated cows and their fetuses; determining the mechanism of BT-viral escape from persistently viremic cattle by C. variipennis; determining the significance of BTV in the weak calf syndrome and the BTV-parvovirus relationship in the disease; determining the location of BTV in persistently viremic cattle, e.g., within a cell-type or in circulating antigen-antibody complexes; identifying different methods of attacking BTV, EHDV, and other orbiviruses by understanding the molecular components of the virions and by using physicochemical parameters rather than experimental animals for antigenic characterization of virus strains; controlling C. variipennis and other vectors of BTV and EHDV by applying ecologic-ethologic-physiologic knowledge without using chemicals or other influences disruptive to the environment.

C Research Approaches. There are many research approaches to providing information necessary to a better understanding of BT disease, its diagnosis, and identification and characterization of insect vectors. Obviously, all of these approaches cannot be pursued simultaneously. However, they are recognized and, as circumstances permit, will be made a part of the ongoing research program. Generally, the approaches fall into the categories of diagnosis, mechanism of infection, immunity, and entomological aspects.

Entomology-related information is of primary importance in understanding and eventually controlling the disease, particularly its transmission and perpetuation among sheep, cattle, and other susceptible animal species. Several research approaches should be pursued.

Quantitate and standardize the soluble antigens used in the AGP test for BT and EHD antibody identification; investigate new serologic and diagnostic techniques for BT and EHD, such as seroenzymatic techniques (e.g., horseradish peroxidase) and immunoelectron microscopy; compare the MDCF, AGP, and plaque reduction neutralization tests for accuracy and sensitivity in detecting BT and EHD antibody; compare the 2 available plaque reduction neutralization techniques for BTV and EHDV antigenic serotyping for accuracy, sensitivity, reproducibility, and facility of universal application; examine available cell lines and chemical additives for cell media (e.g., mitogens, mutagens, sensitizers, and synchronizers) to diagnose BT and EHD infections more rapidly than the 1 to 6 weeks now required; antigenically characterize or serotype BTV-strains by physicochemical, rather than by biologic methods; use serodiagnostic tests in field studies with APHIS to determine the geographic distribution and estimate the economic importance of BT; apply appropriate diagnostic, serologic, and control techniques to other orbiviruses and arboviruses identified as disease problems in ruminants.

Determine the frequency that in utero BTV infection produces teratologic or fetal destructive effects or produces a steady-state viremia in calves that can be transmitted to susceptible ruminants by C. variipennis; virologically follow the pathogenesis of BTV in the genital tract of bulls; determine whether BTV can infect cows and heifers after artificial or natural insemination; determine whether BTV in semen causes abortions or teratologic effects on bovine fetuses; by chemical and enzymatic methods, determine the mechanism of viral escape from BTV carrier animals with C. variipennis; attempt to reproduce weak calf syndrome experimentally with BTV and parvovirus; by using electron microscopy and immunofluorescence, determine whether BTV circulates as antigen-antibody complexes in persistently viremic cattle, or if BTV is located in erythrocytes or bone marrow cells; predict and, perhaps, control the evolution of new, more virulent BTV serotypes; examine the nature, specificity, and avidity of antigen-antibody interactions to explore the mechanism of circulating virus-antibody complexes in BT and immune complex diseases; attempt to artificially block or mimic the autograft effect by chemical and enzymatic manipulations.

Determine the quality, quantity, and duration of antibodies stimulated in cattle and sheep by polyvalent BTV vaccines; establish the effectiveness of polyvalent BTV vaccines in sheep and cattle to the antigenic serotypes of BTV; determine whether attenuated, polyvalent BTV vaccines are teratogenic to fetal lambs and calves; determine the duration of immunity in sheep and cattle to polyvalent vaccines; determine whether vitamin E and selenium can enhance the immunogenicity of BTV vaccines; determine the chemical composition of orbiviruses so that chemical analogs can be used in BT control; use known physical parameters and chemical sensitivities to increase antigenic mass for the production of an immunogenic, safe, multivalent, inactivated vaccine; determine if soluble antigen can be used as a BT immunizing agent for cattle and sheep; by hybridizing viral serotypes, enhance the antigenic determinants for immunity of BTV-vaccine strains to broaden the protection of vaccinated animals to the naturally evolving serotypes.

Develop automated colonization methods to produce a standardized, viable, competitive fly for experimental and field research; define the pathogenesis of BTV infection with C. variipennis and the mechanism by which the fly becomes infected and transmits BTV; determine if transtadial or transovarial infection of C. variipennis occurs with BTV; define the C. variipennis complex so that field and laboratory populations can be compared; define the physiology of normal C. variipennis by using electron microscopy, radiolabelling techniques, enzymatic and chemical assays; initiate a C. variipennis control program with sound waste water management; control BT disease in the field by using a genetically derived population of BTV-resistant C. variipennis; identify other biting or blood-sucking arthropods that can be infected with and transmit BTV and EHDV.

D Consequences of Visualized Technology. Eliminate BTV as a nontariff trade barrier to the export of U.S. sheep, cattle, goats, and germ plasm to other countries; reduce the losses of red meat (lamb, beef, veal) caused by death and poor weight gain or BT- or EHD-infected animals; reduce the losses from wool damage and decreased milk production caused by BT and EHD infection; decrease the time needed to diagnose BT so that an effective vaccination program can be initiated more rapidly to control outbreaks; decrease the incidence of BT and EHD by ecologically compatible methods of C. variipennis control; decrease the ability of C. variipennis to transmit BTV and EHDV to ruminants; by genetically increasing resistance of C. variipennis to BTV or EHDV infection, susceptibility to arboviruses not presently known to be transmitted by Culicoides may be increased; alteration or elimination of the ecological niche that Culicoides occupy may favor the presence of a more noxious pest in that niche; controlling BTV by vaccination of animals and manipulations of the vector would reduce the size of the BT enzootic area in the U.S.; application of the knowledge derived from genetic manipulation to reduce vector susceptibility to BTV could be applied directly to the control of other viruses of veterinary and public health significance; establish the geographic distribution of BT in the U.S. from which to derive realistic estimates on the economic significance of BT on the U.S. livestock industry and the resulting cost

to the consumer of red meat, wool, leather, and dairy products, similar advantages and disadvantages would accrue from the identification, diagnosis, and control of other arthropods and arboviruses; initially, the revelation of persistent bovine BT viremias and BTV in semen will have a negative effect on livestock and semen exports; by recognizing the problem, improved diagnostic techniques will be developed so that U.S. cattle and bovine semen can be certified BTV-free for exportation; by clarifying the role of BTV in weak calf syndrome, control measures can be taken to reduce the losses from repeat breeding in cows and heifers, calf deaths, and lost productivity; by eliminating the bovine carrier state that provides an overwintering mechanism for BTV, there will be a decrease in BT in sheep; demonstration of an escape mechanism for BTV by C. variipennis from carrier cattle will provide a tool with which similar viral diseases of public health significance can be studied and controlled; improved diagnostics for BTV, EHDV, and other orbiviruses; control of BTV without the danger of using live virus vaccines; provide a model for viral serotyping that does not require the use of experimental animals; provide methodology to attack other virus diseases of veterinary and public health significance; nonchemical control of Culicoides and BT; provide a model for the control of other insects; provide an effective control method for use in emergency situations based on knowledge of C. variipennis physiology and enzyme systems.

E Potential Benefits. The potential for export of purebred breeding cattle and germ plasm to countries that presently refuse U.S. cattle and semen for artificial insemination could amount to millions of dollars. It has been estimated that 10,000 cattle could be exported yearly if BT were not a danger to the sheep industries of other countries. If assumed that the value of a purebred animal is $1000, annual exports of live animals could be $10,000,000 per year.

Germ plasm from U.S. cattle is exported to certain countries and the market could be expanded if the danger of BT were eliminated. If 50,000 vials of semen at $10 per vial were exported per year, the value would be $500,000 per year.

Although the U.S. is essentially a meat importing country, export of prime or choice beef does occur; e.g. to Japan. The export market for high-quality U.S. beef could be expanded to the beef eating populations of the world--New Zealand, Australia, United Kingdom--if BT were not a problem. If 10,000,000 pounds of beef at $1.00 per pound were exported, the value would be $10,000,000 per year.

Bluetongue losses in cattle and sheep must be measured in parameters that include the loss of red meat, loss of dairy products, damage to wool and leather, expenses of veterinary services and drugs, loss of breeding efficiency, and death of animals. Since no field surveys have ever been conducted in the U.S. for BT, economic estimates must be considered as guesses.

Assuming: The number of cattle in the 22 Western States where BT is most prevalent is 90,200,000, 5 percent of the herds are affected each year, morbidity averages 5 percent, 1 percent of infected cows abort or produce calves with congenital anomalies, cost of treating infected cattle is $18 per head, average loss from an aborted calf is $75, the annual BT loss in U.S. cattle could be:

Number of cattle affected:	.05 x .05 x 90,200,000 = 225,500 head
Number of calves lost:	50% of all cattle are cows = 45,100,000
	.05 x .05 x .01 x 45,100,000 = 1128 calves lost
Cost of treatment:	22,500 x $18 = $4,059,000
Calf loss:	1128 x $75 = $84,560
Total cattle loss per year	$4,143,560

Assuming: The number of sheep in the 22 Western States is 12,643,500 that 10 percent of flocks are affected, morbidity of 30 percent of flock, an average weight loss of 15 pounds per sheep, since lambs are most severely affected, assume 35 cents per pound for weight loss, fleece value is decreased 10 cents per pound from damage to the wool fiber, estimated 1975--average value per head is $32.70, mortality is 5 percent of infected sheep, the annual loss in sheep would be:

Number of sheep affected:	.10 x .30 x 12,643,500 = 380,000 head
Number of sheep lost:	380,000 x .05 = 19,000 head
Morbidity loss:	380,000 - 19,000 = 361,000 head
	361,000 x 15# x .35 = $1,895,000
Mortality loss:	19,000 x $32.70 = $621,300
Wool loss:	361,000 fleeces x 8# x .10 loss = $288,000
Vaccination costs:	609,000 doses x .25 = $152,250
Total sheep loss per year	$2,956,550

Total sheep and cattle loss: $7,100,110 per year

Potential benefits of the research program described have been calculated from best estimates and should be expected to amount to about a 30 percent reduction of the presently experienced losses in approximately 10 years. The recommended program expansion will reduce that time period by 2 to 3 years.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	1.9	$256,000	3.9
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		7±

The time required to achieve the technological objectives could be decreased by 2 to 3 years by increasing the staff by 2.0 SY's, by improving and expanding the existing facility or by construction of a new laboratory, by adding 7 support personnel, and by increasing available funds to keep pace with inflation to absorb the rising costs of expendable and non-expendable items and to adjust for salary increases.

Horses

1.1 Equine Encephalomyelitides

A Current Technology. There are no diseases more alarming or more brutal to domestic animals and man than the viral encephalitides. Three immunologically distinct, but related, virus complexes are generally associated with equine viral encephalitis. These viruses, eastern equine encephalomyelitis (EEE), western equine encephalomyelitis (WEE), and Venezuelan equine encephalomyelitis (VEE), are classified as togaviruses and are transmitted by bloodsucking arthropods, primarily mosquitoes. Epizootiologically, these agents are insect-transmitted viruses, or arboviruses. Epizootics of EEE, WEE, and VEE have occurred repeatedly among horses of the U.S. and often have caused concurrent disease in people.

The rapid increase in the equine population of the U.S. is creating a situation highly conducive to the occurrence of epizootics of encephalomyelitis similar to those that occurred during the 1930's when tens of thousands of horses died from EEE and WEE, annually. The 1971 outbreak of VEE in Texas exemplifies the potential seriousness of the situation. Although confirmed horse deaths from VEE were less than 1000, and horse illnesses were only in the thousands, the cost of the control campaign was more than $30 million, excluding the cost of the 2,843,000 doses of vaccine used in 19 states. In terms of the emotional anguish of concerned pleasure horse owners and of the suffering of infected people, no economic parameters can be drawn.

The diagnosis of equine viral encephalomyelitis is made from clinical signs of illness, by isolating and identifying the viral agent, and by identifying the presence of virus-specific antibodies in the serum of infected horses. Initial clinical signs of fever and leukopenia are observed in horses within 24 to 48 hours after being bitten by an infected mosquito. The first signs indicative of clinical encephalitis do not occur until 2 to 4 days later. Horses become anorectic and psychically depressed. Some horses experience profound depression, blindness, deafness, paresthesia, and eventually collapse and die. Other horses experience a "furious" illness with violent convulsions; they have a tendency to walk in circles, and paddling with the legs occurs when the horse becomes recumbent. Infected horses may die quickly, experience mild to severe clinical disease or may remain clinically normal.

The togaviruses can be isolated from the blood or brains of infected horses by inoculating specimens into cell cultures, embryonating chicken eggs, suckling mice, or guinea pigs. The viral antigen that is isolated can be identified as EEE, WEE, or VEE virus by hemagglutination-inhibition, complement-fixation, or plaque reduction neutralization techniques.

Serological confirmation of togavirus infection can be made by using the same 3 diagnostic tests listed above. It is essential, however, that paired serum samples be tested to demonstrate an antibody titer rise before making a diagnosis of encephalomyelitis virus infection. These serum samples should be taken early in the course of the disease and 7 to 14 days later.

The control of equine encephalomyelitis involves a multidirectional approach since the epizootiology involves a host (horse, mules, and donkeys), mosquito vectors and any one of 3 togaviruses (EEE, WEE, VEE). Effective vaccines are available for EEE, WEE, and VEE viruses and have significantly reduced the incidence of equine encephalomyelitis when used in a planned vaccination program. During epizootics, mosquito control measures, including the use of insecticides, have proved effective and essential.

Western equine encephalomyelitis was the first of the equine encephalomyelitis viruses to be described. The late K. F. Meyer and his associates isolated the virus from horses with encephalomyelitis in 1930; eight years later, WEE virus was identified as a lethal human pathogen. Epizootics and associated epidemics have occurred frequently since then. Initially, WEE virus was considered to be present only west of the Mississippi River, but it is now apparent that the virus exists throughout the U.S., and has been isolated from Canada to Argentina in the Western Hemisphere.

Western equine encephalomyelitis has a very wide natural host range that includes man, equines, squirrels, mice, rats, deer, pigs, garter snakes, tortoises, and birds. In birds, a nonfatal, high concentration virema occurs.

Birds are considered very important as the basic reservoir in the natural cycle of the disease. It is believed that man and horses are tangentially infected, and because of the low concentration of virus in these hosts' blood, they are considered to be dead-end, indicator hosts.

Many species of mosquitoes have been proved susceptible to infection with WEE virus. To prove vector status, however, virus transmission must be shown. Culex tarsalis, a mosquito that feeds on mammals and birds is considered to be the principal vector of WEE in the U.S.

The epidemiology of WEE in the U.S. supports viral persistence in an, as yet, undefined overwintering mechanism. Virus has been isolated from C. tarsalis collected in the winter, but survival of adult mosquitoes through winter is poor. Overwintering of WEE virus in vertebrates is a realistic possibility. Birds have been experimentally demonstrated to be viremic for up to 10 months. Garter snakes and Texas tortoises have been demonstrated to be viremic after winter hibernation, as have naturally infected small mammals; e.g., squirrels, mice, and a rat.

Although antigenic variation has been demonstrated for WEE virus, there has been no correlation with pathogenicity for horses or man. Experimentally, WEE virus is lethal for intracerebrally inoculated mice, guinea pigs, hamsters, rabbits, rats, monkeys, cotton rats, equines, pigs, calves, puppies, and field mice; cats and sheep are resistant.

Vaccination of horses has produced a significant reduction in epizootics. A Formalin-inactivated WEE virus vaccine has been produced in chicken embryos. This is generally administered as a bivalent vaccine with EEE virus.

Eastern equine encephalomyelitis virus was isolated from a horse brain in 1933 during an epizootic in the eastern U.S. It was confirmed as a lethal pathogen of man in 1938 during an epidemic in Massachusetts. Infection produces a more severe, more frequently fatal encephalitis of man and horses than WEE. The virus is distributed on the Atlantic side of the Americas from northeastern U.S. to Argentina. Small, but usually severe, epidemics have occurred in different localities, often preceded and accompanied by epizootics in horses. Yearly epornitics occur in pheasants in the northeastern U.S., where it is a significant economic problem.

The natural reservoir of EEE virus is unknown; however, isolations from numerous species of wild birds suggest that birds are the virus reservoir. As with WEE virus, EEE virus appears to cycle naturally in birds, probably with a mosquito vector of the genus Aedes. Horses and man appear to be tangentially infected during epornitics, and due to the low concentrations of viremia produced from infection, they are considered to be dead-end, indicator hosts of the virus.

The range of experimental and wild animals that develop a fatal infection after intracerebral inoculation is large and similar to WEE. In addition to the animals listed for WEE, pigeons, ducks, hens, hedgehogs, sheep, cats, and dogs are susceptible. The EEE virus is potentially the most serious pathogen. Researchers must be vaccinated with Formalin-inactivated, chicken embryo origin vaccines. Similar vaccines are used in horses.

Venezuelan equine encephalomyelitis virus was first isolated in Venezuela in 1938 from a horse brain. Major epizootics, often with accompanying epidemics, have occurred periodically in northern South America, but until 1969, no confirmed epizootic of VEE had ever been reported north of Colombia. In 1969, a major epizootic-epidemic began in Central America that progressed as far as Texas before an hemispherical effort costing millions of dollars succeeded in halting the relentless progress of the disease. Millions of doses of an attenuated VEE virus vaccine developed by the U.S. Army Medical Research Unit were used in horses from Costa Rica to the U.S. Aerosol spraying with ultra-low volume insecticides was finally used with the vaccine to avert this major threat to U.S. equines. The cost of the U.S. epizootic in terms of horses quarantined, races, rodeos, circuses, and carnivals stopped is inestimable.

Venezuelan equine encephalomyelitis is a highly fatal disease of horses and man, especially in children and elderly adults. Experimentally, the virus is pathogenic by intracerebral inoculation for the mouse, guinea pigs, rabbits, chicken embryos, rats, dogs, cats, sheep, equines, and goats. By peripheral routes of inoculation, only equines are lethally infected; dogs experience a variable severity of illness.

By using a short incubation hemagglutination-inhibition test, 4 subtypes of the VEE virus complex have been identified. Within subtype I, at least 4 variants have been identified. These subtypes and variants have been associated with very different virulence, physicochemical, and ecological characteristics.

The epizootiology of VEE viruses has been more adequately defined than that of EEE and WEE. Equine epizootics have been caused by variants A-B-C of subtype I only. Initial studies that suggested 3 epizootic variants have been difficult to reproduce. The epizootic variants can be isolated only during epizootics and are highly lethal for equines. Humans are tangentially infected, occasionally with fatal consequences; epidemics follow onset of equine disease by about 2 weeks. Epizootics occur in rangeland that experiences a prominent dry season; many species of mosquitoes and a biting fly, Simulium spp., have been incriminated as vectors of the virus. The origin of epizootic VEE variants is unknown and during inter-epizootic periods, the virus cannot be found in nature. It has been hypothesized that epizootic variants persist in mammalian reservoirs until a combination of suitable vectors and susceptible equine hosts is available to support an epizootic. Another realistic possibility is that epizootic variants periodically arise by mutation from enzootic variants when conditions favor epizootic spread.

In contrast, enzootic variants that are apathogenic for horses can be detected at any time in sylvatic cycles that involve rodents and Culex melanconion spp. mosquitoes. These sylvatic cycles are found in open swamps or wet jungles throughout Latin America. Sylvatic cycles of VEE variants in subtype I are located in reasonable proximity to areas where epizootics of subtype I variants have occurred. Subtypes II, III, and IV have never been associated with epizootics, although all sylvatic VEE strains are pathogens of man. A sylvatic focus of VEE is found in the Florida Everglades where subclinical and overt infection of humans has occurred. The epizootic VEE variant does not appear to have persisted in the U.S.

Many realistic questions were asked about the live, attenuated VEE vaccine before it was used in the U.S. in 1971. The vaccine was developed by the U.S. Army from an exotic, equine virulent variant of VEE by passing the virus in fetal guinea pig heart cells. It has been shown that the vaccine is safe and effective. An added benefit of equine vaccination is that human infection is controlled by stopping the disease in horses. Equines are protected for at least 18 months and, perhaps, for life. Neutralizing antibody to vaccine and epizootic strains of VEE persist for at least 30 months. The vaccine virus does not revert to a more virulent form by artificial horse-to-horse transmission and does not appear to cause more than a transitory illness in vaccinated equines. Simultaneous or sequential vaccination with the attenuated VEE vaccine and the inactivated, bivalent EEE-WEE vaccine stimulates a more marked antibody response to all 3 viruses in equines. Preexisting natural EEE or WEE antibody appears to interfere with the magnitude of the antibody response of equines to VEE vaccine, but does not appear to affect the immunity to virulent VEE virus challenge.

The attenuated vaccine was developed to protect U.S. military personnel against VEE virus used as a tool for germ warfare. It has been used for a decade to protect at-risk laboratory personnel who were working with the virus. Venezuelan equine encephalomyelitis virus has caused hundreds of laboratory-acquired infections and is dangerous by the aerosol route of infection. It can cause a serious debilitating illness in man.

During the outbreak of VEE in Texas, horses in California were monitored for encephalomyelitis. It was discovered that many cases of clinical encephalomyelitis were not due to EEE, WEE, or VEE viruses, and were undiagnosed as to etiology. A serological study of equines was conducted with arboviruses isolated in California and it was shown that antibody to at least one other virus, Maindrain, was present with sufficient frequency to suggest that investigation into the effects of this virus on equines was warranted. In addition, Maindrain virus has been isolated from horses with clinical encephalitis. The effects of other arboviruses, e.g., Buttonwillow, Lokern, St. Louis encephalitis, California encephalitis, Turlock, Modoc, Kern, and other togaviruses are also unknown.

The physical characteristics of the group A togaviruses or alphaviruses that include VEE, WEE, and EEE are similar and quite distinct from all other virus groups. With the electron microscope, the virions appear as fuzzy spheres with surface projections and an outer envelope.

The alphaviruses are serologically related, have a single-stranded ribonucleic acid (ss-RNA) genome, and produce hemagglutinins. Formalin is used to inactivate togaviruses for vaccine production. Inactivated vaccines for VEE, however, have proven dangerous and ineffective. Numerous outbreaks of VEE have resulted in horses from the use of incompletely inactivated virus that cannot be detected by safety tests, except in humans and horses.

Physicochemical methods can be used to concentrate and purify viruses. By increasing antigenic mass of VEE virus and by understanding chemical sensitivities, an effective, safe, immunogenic, inactivated virus vaccine can be produced to be used in a trivalent WEE, EEE, VEE virus vaccine.

Recently completed studies have established a VEE viral molecular weight of 61 million, a viral sedimentation rate of 22 x 10^{-13} sec., a buoyant density of 1.178, and a partial specific volume of 0.80 m/gm. By using these data, nonbiological, chemical, and physical methods of antigenic characterization among variants and subtypes may eliminate the need for experimental animals for serotyping. Characterization of the viral genome may permit viral hybridization for developing new vaccine strains of alphaviruses and for characterizing and even predicting the emergence of new variants.

Many species of mosquitoes have been incriminated in the transmission of the viral encephalomyelitides. Very few species, however, have been conclusively demonstrated to transmit these viruses to equine hosts. For laboratory studies, potential vector species must be reared in the laboratory in large numbers without the need for artificial copulation, and for the work to be significant, the colonized populations must be relevant to field populations. Since the vector is the only practical means for togavirus transmission, an understanding of the physiology, ethology, and ecology of the vector species is necessary to attack the problems of chemically compatible control methods for the vector and, subsequently, for equine encephalomyelitis.

B Visualized Technology. Facilitate the differential diagnosis of the causes of viral equine encephalomyelitis by: Examining the pathogenesis of EEE, WEE, and VEE, and other arboviruses in horses; characterizing the quantity and quality of the serological responses; establishing the vector status of various species of mosquitoes, evaluating alternative methods of disease control and vaccines, investigating and comparing the relationships between antigenic variants of VEE, identifying unique methods of attacking EEE, WEE, VEE, and other togaviruses by understanding the molecular components of the virion and ss-RNA genome, and controlling of mosquitoes and other vectors of EEE, WEE, VEE, and other arboviruses that cause equine encephalomyelitis without using environmentally disruptive methods.

C Research Approaches. Develop improved diagnostic tests for the viral equine encephalomyelitides; study facets of the pathogenesis of equine encephalomyelitis that deal with the cause of fatal encephalitis, such as antigen-antibody complexes; examine the immunologic relationships of EEE, WEE, and VEE in equines; evaluate interference of cross-protection of WEE, EEE, and VEE in equines; determine the efficacy of inactivated trivalent encephalomyelitis vaccines in equines; develop immunofluorescence, seroenzymatic, and radiolabelling techniques to speed the identification of viral etiologic agents and to study the pathogenesis of viral infections; determine whether the live, attenuated VEE vaccine virus can revert to virulence by serial-cyclic passage in horses and mosquitoes; determine VEE virus infection rates in potential vector species; establish vector status of mosquito species by demonstrating ability to transmit virus to susceptible hosts; determine the pathogenic potential of other togaviruses and arboviruses for equines; explore the relationships of humoral antibody and cellular immunity to the mechanism of encephalitis and to the long duration of togavirus-stimulated immunity; manipulate sylvatic variants of VEE to enhance virulence for horses to explain the origin of VEE epizootics; determine the chemical composition of togaviruses so that chemical analogs can be used in control and treatment of encephalomyelitides; use known physical parameters and chemical sensitivities to increase antigenic mass for the production of safe immunogenic, inactivated vaccines; antigenically characterize or serotype togavirus variants by physicochemical rather than by biologic methods; develop automated colonization methods to produce a standardized, viable, competitive mosquito for laboratory and field research; by using selected populations of Aedes aegypti, determine whether genetics influences vector capacity; define the pathogenesis of VEE sylvatic and epizootic strains for selected mosquitoes; establish the mosquitoes species responsible for togavirus transmission in equine encephalomyelitis.

D Consequences of Visualized Technology. Facilitate the international movement of equines; prevent the loss of racing, breeding, working, and pleasure horses; provide a means to control the spread of viral equine encephalomyelitis in the U.S.; increase the pleasure derived from equestrian activities; prevent equine and human suffering from these lethal, dreaded diseases; develop effective, ecologically compatible methods of insect control; reduce human and animal suffering and discomfort due to mosquito pests; produce safer, more effective vaccines for EEE, WEE, and VEE; decrease the time needed to diagnose the etiology of viral equine encephalomyelitis to reduce the danger to other equines and man; determine the origin of encephalomyelitis epizootics so that the reservoir of nidus of infection can be attacked and eliminated; explain the reasons for and mechanism responsible for the long duration of immunity stimulated by togavirus infection or vaccination; eliminate the dangers associated with the use of Formalin-inactivated VEE vaccines.

E Potential Benefits. In view of the rapidly changing economic situation and the current rate of inflation, a projection through 1985, or even through 1980, is unrealistic. It is impossible to place a dollar value on human suffering or happiness. If control or elimination of viral equine encephalomyelitis prevented the death of a single child, then reasonable expenditures to attack the disease are warranted.

It has been estimated that in 1975 the racing horse population in the U.S., including thoroughbreds, standardbreds, and quarterhorses, consisted of 100,000 active racers and 250,000 to 300,000 breeding mares and studs. It is estimated to cost $15,000 per year to maintain a race horse. In 1973, $7,000,000,000 was wagered in parimutuel betting at racetracks in the U.S.; this yielded $533,500,000 in revenue to the States. The loss of a month of racing in the U.S. due to an encephalomyelitis quarantine could cost the States $44,450,000 in lost revenue.

There are approximately 1,500,000 nonpleasure horses (ranch horses, farm horses, show horses, and police horses) and an estimated 6,000,000 pleasure horses in the U.S. It costs $200 to $300 per year to maintain the backyard pleasure horse. Horsemen, both young and old, derive sentimental, educational, and recreational value from the care and ownership of their horses. The total potential losses that might be attributable to an outbreak of one of the equine viral encephalomyelitides are inestimable.

It has been estimated that land valued at $2,000,000,000 is used to support horses per year. Approximately $6,000,000,000 has been invested in the horses themselves and approximately $6,000,000,000 is spent yearly on feed, tack, and veterinary services.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	3.5	$425,000	4.5
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		7±

The time required to achieve the technological objectives could be decreased by 2 to 3 years by increasing the staff of the laboratory by 1.0 SY, by improving and expanding the existing facility or by construction of a new laboratory, by adding 3 support personnel, and by increasing available funds to keep pace with inflation to absorb the rising costs of expendable and nonexpendable items and to adjust for salary increases.

1.2 Equine Infectious Anemia (EIA)

A Current Technology. The immunodiffusion (Coggins) test developed in 1970 has served as a laboratory test in detecting EIA infection in horses and is useful in epidemiological studies. An improved diagnostic EIA antigen produced from infected cell cultures and developed by ARS scientists has provided a more standard and economical reagent that will enhance the usefulness of the test. The incidence of EIA infection for FY 1974, based on the Coggins test, was 2.71 percent nationwide, but it varied widely from state-to-state. Prior to development of the Coggins test, there was no reliable information on the incidence of infection. It is now known that the highest incidence of infection appears to be in the South, particularly in states bordering the Gulf of Mexico. Testing bands of horses at six-month intervals has been successful in controlling EIA in selected areas of Louisiana. This serves as a model for an effective control program. The common horse fly, Tabanus fuscicostatus, also studied in the program, appeared to be the single most important vector in the transmission of EIA virus. Equine infectious anemia can be eradicated by a control program, using available technology. Compulsory testing of all horses involved in interstate shipment or public events and incentives for individuals with home-stabled horses will bring most horses into the control program.

There have been numerous attempts over a long period of time and in several countries to develop vaccines against EIA and none have been successful. Basically, there are two types of viral vaccines; one utilizes an inactivated virus and the other an attenuated or modified virus; and both of them have been tried with EIA. Since horses affected with EIA develop antibodies against the virus, it is logical to assume that the virus would be eliminated, but this is not the case. Affected horses continue to harbor the virus, sometimes in an inapparent form, and this cannot be terminated or prevented by any of the vaccines. Past experience with the often dramatic effect of vaccines has placed a great deal of emphasis by the general public on the availability of an EIA vaccine. It is not surprising, therefore, that private companies are taking a lead in this phase of EIA research. Lack of progress in the development of a vaccine may be due to inadequate basic knowledge of how the virus can survive in the host.

Virus persists in an infected animal through a mechanism or combination of mechanisms that is currently explained by at least three theories. It is postulated that virus can persist in an infected animal by maintaining an intracellular existence, thus not becoming exposed to the inactivating effect of antibodies. Another explanation is the probability of antigenic drift of the virus. During residence of the virus in an infected animal, the antibody response of the host will be directed against a specific antigen in the virus. Intracellular virus escaping the action of antibody may undergo slight antigenic changes and not be affected by the antibody as it becomes extracellular. This slightly antigenically altered virus becomes the predominant type until the antibody response of the host

represses it. Through constant changes in the antigenic composition, a virus may persist in the presence of antibody. A third explanation for the persistence of virus in an infected animal is the survival of virus in an antigen-antibody complex. The antibody induced by the virus combines with the virus and builds up aggregates, some of which are trapped in small blood vessels. The virus is not completely inactivated, and when the resistance of the host decreases due to stress or there is a decrease in antibody excess, new cells become infected, producing a recycling of the infectious process.

There is some evidence that all three theories operate alone or in combination. New technology for carrying out definitive experiments is needed, but it has been hampered by the inadequacies of an in vitro cell culture system. Research in this area has not been supported by industry, since it is a long-term project with no immediate prospects of remuneration. Institutions involved with basic problems in virology are directing considerable effort to the study of related disease conditions.

Close to 100 percent of all horses are infected with equine herpes-2 and over half appear to have been infected with equine herpes-1 (equine abortion or equine rhinopneumonitis virus). Approximately 25 percent of the horses have been infected with equine herpes-3. Only equine herpes-1 and herpes-3 appear to produce recognizable disease syndromes, but equine herpes-2 interferes with investigational procedures used in EIA research. The only cell culture system where EIA virus produces a cytopathic effect utilizes horse leukocytes. All titrations of virus and neutralizing antibody involve this system, but leukocytes infected with equine herpes-2 are not capable of surviving in cell cultures. Foals handled by a definite procedure at birth (SPF animal procedures) can often be raised as equine herpes virus-free, but they must be constantly monitored for infection. This may involve any of the equine herpes virus types and accurate identification of the types involved is essential. Also, we are unaware of how equine herpes virus infection at different stages may influence an experimental infection with EIA virus.

B Visualized Technology. Adequate quarantine procedures must be put in use for stabling the infected mare and isolating the newborn foal. Vaccine developed from the EIA virus adapted to an equine cell line will be tested for its efficacy in immunizing horses without producing carriers. An effective vaccine could be used after a preliminary test to prove a horse free of EIA and the eradication program could be phased out. By discovering the mechanism whereby virus persists in an infected horse, it will be possible to explain why antibodies seem ineffective in eliminating or preventing an infection. This will provide a basis for new technology needed to produce an effective vaccine. Intercurrent viral infections in experimental horses, in which there is an incidence close to 100 percent with equine herpes virus-2, have hindered research on EIA. Foals for experiments will be produced virus-free by procedures developed for SPF animals. Investigations on the relatedness of the three equine herpes virus types will lead to quicker diagnostic capabilities and help to elucidate the mechanism of herpetic encephalitis, which is also a serious disease in man. Development of an improved vaccine against equine herpes-1 (equine abortion) to control intercurrent viral infections will be an added benefit.

C Research Approaches. Can the Coggins test be modified so the results are more quickly obtainable, and can it give more definitive results with weak antiserums? Can an area be kept completely free of EIA in a pilot plan by the process of testing and eradicating horses reacting positively? What vectors are mainly instrumental in the transmission of EIA in different areas? Do EIA viruses multiply in the vector or are they simply mechanical carriers? What percentage of the noninfected mares served by infected stallions become positive in the Coggins test, and does the fetus become infected? What is the maximum period of time that must be allowed for EIA infection to express itself in a foal obtained from an infected mare? Is "catching" a foal during natural birth as effective as birth by Caesarean section in obtaining an EIA-free foal from an infected mare? Can equine dermis cells infected with EIA virus be inactivated and retain their antigenicity so that a good antibody response results when they are inoculated into a horse? Can a protective mechanism against infected cells be demonstrated by a cytotoxic reaction or an in vitro antigen-antibody test? What is the duration of protection induced in a horse? Will this approach to vaccination be effective against all strains of EIA virus? What are the important antigenic components of an EIA virion that will induce production of the desired protective antibody? Can all possibilities of antigenic drift be found in a relatively few isolates of EIA virus? What is the most accurate method of measuring antibody and correlating it with protection? Does the incorporation of an adjuvant enhance the antigenicity sufficiently to justify its incorporation in a vaccine? Which is the best adjuvant for the purpose? Can infected and inactivated equine dermis cells be incorporated with inactivated virus to produce a combination vaccine having greater antigenicity than either one above? Can characteristics of the virus be modified by growing it in foreign host cells so it no longer behaves typically when reintroduced into the natural host? Will the virus still induce immunity? Can antibody against infected cells be produced in the host that will terminate the carrier state? Can virus reisolated at different intervals of time from a latently infected host be shown to differ antigenically? This would constitute evidence for antigenic drift. Can antigen-antibody complexes be produced experimentally in which both active virus and antibody are demonstrated? Can horses be sensitized by inoculating inactivated, infected-cell antigen so they will respond quicker to a modified live virus and be made immune? Which cell type in the infected horse harbors the persistent virus? Equine herpes virus-free horses will be obtained by a modified SPF type of procedure and raised in isolation. Specific immunodiffusion antigen for each of the equine herpes virus types will be prepared in equine cell lines. Specific antisera against each type will be prepared in horses. These horses must be free of herpes-2 prior to hyperimmunization. All herpes virus-free horses will be bled periodically and their sera will be tested for antibody to confirm their noninfected status. Horses will provide an unlimited supply of leukocytes that can be used in cultures for the titration of EIA virus and neutralizing antibody. The neutralization index of sera from an EIA-infected horse collected over a period of time when tested against the original infecting virus and the extant virus will indicate the degree of antigenic drift. The relatedness of all 3 types of equine herpes virus will be compared by the double and radial immunodiffusion techniques. Procedures for developing an alternative and possibly superior antigen for vaccination of horses against equine herpes virus-1 will be examined.

D Consequences of Visualized Technology. Valuable horses will be lost through implementation of an EIA eradication program. Some lines can probably be maintained by rearing non-EIA-infected foals from EIA-infected mares. Many horses are family pets and many owners will be uncooperative if it involves destruction of pets.

There will be a decrease in the horse population and the cost of horses will increase. There will be an inequitable distribution of profits and losses among the horse owners resulting from the EIA eradication program.

Utilization of vaccines will interfere with the Coggins test used for detecting EIA. The demand for a vaccine, however, makes research in this area essential, but there is no preliminary evidence available that indicates any hope for success.

The cost of developing, testing, and applying a vaccine will be considerable and may require a continuous practice on the part of horse owners. Eradication of EIA by testing and removing reactors may be more costly, initially, but less expensive over a long period of time.

After eradication of EIA, there will be an easing of restrictions on the interstate movement of horses. Consequently, there will be more horse shows, etc., involving better quality horses.

An effective vaccine against EIA would have greater acceptance by horse owners than eradication. All of the benefits resulting from eradication could be duplicated by successful vaccination.

Discovery of the mechanism that operates and allows infected horses to remain virus carriers will be a great help to medical science. Many viral diseases follow a pattern similar to EIA, and any new technology developed in this area may be directly applicable to controlling them.

A better vaccine against equine herpes virus-1 (equine abortion) resulting as a by-product on the study of intercurrent infections in horses will be especially useful.

E Potential Benefits. The animal loss from EIA due to death and debilitation was estimated at $145,791,125, in 1974, while the annual cost for conducting an eradication program is estimated at between $14,000,000 and $15,000,000. Thus, in ten years of operation, the eradication program will be equal to losses incurred in one year. After ten years, when EIA is under control, the savings accruing each year to horse owners will be equivalent to the cost for ten years of an EIA control program. A potential loss of breeding studs is anticipated, but the monetary loss cannot be quantitated. Foals from an infected brood mare, however, could, in some cases, be salvaged at an additional cost of $1600 per animal. Substituting a vaccination program for testing and eradication could, after ten years, save the entire cost of an eradication

program. An unknown factor is the possibility of a successful vaccination "breakthrough" by industry that could contribute all of the essential technology without any cost for ARS. Potential benefits are indirect since they will facilitate the development of a vaccine and basic research on EIA. A benefit not possible to quantify is the acquisition of basic knowledge on virus persistence as it applies to several other viral diseases. Several benefits, in addition to facilitating research on EIA, will be realized from achieving the technological objective. It may contribute to the understanding of herpetic encephalitis and also result in a safer vaccine against equine abortion caused by equine herpes virus-1. This last benefit could be expected within five years and result in a saving of several million dollars per year to horse owners.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	3.0	$520,600	4.0
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		8

Support for EIA research also originates from several horse associations, foundations, private industry, and university budgets. The total amount is unknown.

Factors limiting research progress is the need for new technology, principally in two critical areas. There is a need for basic knowledge on the ineffectiveness of the immune mechanism in carriers and obtaining reliable experimental horses for source materials. Expanded in vitro studies using leukocyte cultures for titrating virus and antibody are essential, and the only reliable sources of leukocytes are from virus-free horses produced by SPF procedures. Extramural support by ARS should be directed into facilities that have demonstrated capabilities in critical areas.

1.3 Helminths of Horses

A Current Technology. Equine helminthic diseases are insidious and ubiquitous, in that many of these infections result in slow debilitation and a capricious appetite, but without gross evidence of clinical disease. Equids are hosts of more species of helminths than any other domestic animal. In the U.S., equine nematodes or roundworm parasites are represented by 26 genera and 71 species, and cestodes or tapeworms by 3 genera and 4 species. In addition, 3 species of bot fly larvae occur commonly in the alimentary tract of horses. These parasites that occur in varying degrees in all horses produce various debilitating effects and often death. The effects of these parasites usually are more insidious than those associated with infectious disease organisms, and antemortem diagnosis is often difficult or impossible.

Three species of large strongylids (Strongylus vulgaris, S. edentatus, S. equinus) occur in American equids and are major causes of disease. Both the adult parasites, which occur in the large intestines and ingest blood and intestinal tissues, and the immature stages, which migrate to various locations in the abdominal organs and induce a variety of serious lesions, are extremely damaging to the health of horses. Particularly serious are thrombi and aneurysms induced in intestinal and other major arteries. These lesions often result in arterial blockage, rupture, and intestinal or other infarctions. In this connection, it has been estimated that S. vulgaris, the primary species involved, is responsible for as much as 90 percent of all equine colic. Other pathologic effects include hematomas, necrosis, and nodular tumors in the internal organs produced by migrating immature larvae. Unexplained migrations by immature large strongylids are exemplified by the recovery of such parasites from hemorrhagic lesions in cryptorchid or undescended testes and elsewhere. S. vulgaris has long been considered the most pathogenic of the three species of Strongylus, but the other two species also are responsible for serious losses. Details of the normal and abnormal migrations of these parasites in the internal organs of horses have not been fully elucidated. In addition to the three species of large strongylids, there are some 75 additional species of nematodes, cestodes, and stomach bots that contribute to the overall helminthic disease problem in American equids. All require detailed investigation with regard to their life cycles, pathogenicity, epizootiology, treatment, and control.

It is known that infections of the small stomach worm, Trichostrongylus axei, will readily transfer between horses, cattle, sheep, goats, and, occasionally, man. Also, the intestinal threadworm of horses, Strongyloides westeri, may occur in pigs. Horses are undoubtedly exposed also to helminths of other domestic animals that may be responsible for unrecognized disease conditions. Horses are closely associated with man in his recreational pursuits and, therefore, become potentially more important in the total epizootiological picture of disease in both man and horse.

Since the USDA discontinued most work on helminthic diseases of horses more than a quarter of a century ago, there is a special need to resume these studies, using the latest techniques and principles for helminthic disease research.

Improved new broad-spectrum anthelmintics for use in equids to control some of the helminthic infections mentioned above are introduced from time-to-time by industry for laboratory and field evaluation. However, no available drug has any effect on migratory larval stages of equine helminths that often produce the most damaging effects in these animals.

B Visualized Technology. The development and evaluation of selective chemical agents effective in the removal of worm parasites from horses and advanced knowledge of treatment of conditions resulting from parasite infections of horses can have a marked influence on the reduction of losses caused by helminthic diseases. New information on the characteristics of helminthic diseases in horses, their epizootiology, and basic biology can be expected. Advances in these areas will appreciably reduce their incidence and associated danger to human health.

C Research Approaches. Basic and applied research are required to develop and evaluate chemical agents and measures for removing worm parasites from infected horses and for minimizing the exposure of grazing animals to infective stages on pasture, to characterize the physical and chemical nature of the helminth parasites and the physiological parasites of the host-parasite relationship, and to develop the methodology for the prevention and treatment of helminthic diseases.

Develop and evaluate selected chemical agents (antiparasitic) for the treatment of helminth parasitism of horses: What helminth species are susceptible to the test chemical? How effective is the chemical against each parasite species (percentage removal)? What is the most feasible regimen of use (pretreatment preparation, optimum dose, method of administration, post-treatment care)? What is the toxicology of the chemical (signs of intoxication, minimum lethal dose, effective antidotes, gross pathology, histopathology)? What are the indications and contra-indications for field use? How does the chemical exert its anthelmintic effect--what is the mode of action? Do drug resistant strains of equine helminths occur or develop in the field, and with what kinds of anthelmintics is such drug resistance associated?

Determine physical and chemical nature of the parasites: What is the morphology, morphogenesis, and systematic status of each of the parasites? What are the physical and biochemical requirements for growth and development of the parasites? What are the metabolic products of growth and development as related to pathogenesis and immunogenesis?

Ascertain the physiology of host-parasite relationships: What is the life cycle of each parasite? What genetic factors are responsible for natural resistance or susceptibility to helminthic disease and for host specificity?

Investigate nonchemical (biological) control measures and develop possible methods for their use in the prevention and control of helminthic diseases: What systems of management can be used effectively to prevent acquisition of helminthic infections. What is the relationship between infection and antibody production and immunity? Can methods of attenuation be used to produce live vaccines? What is the genetic variation among parasite populations?

D Consequences of Visualized Technology. Losses caused by morbidity and mortality in foals, cost for management and medication for helminth-infected horses can be appreciably reduced. Knowledge and technology gained can also lead to significant reductions in losses from helminthic diseases in other classes of livestock. In addition, land conservation and recreational resources can be significantly enhanced to the benefit of the public.

E Potential Benefits. The value of some 9 million equines in the U.S. approximates $4.5 billion, and the annual business income in the horse industry is estimated at $7.5 billion. The incredible regrowth of the horse industry in the U.S., and the redistribution of this new population of animals, have resulted in strong representations by horse associations and other equine-oriented groups for an effective research program on helminthic diseases of horses. The regulatory services of USDA have become more and more involved in the management of parasitic disease outbreaks in equine animals, and hence need the backing of an adequate research program. Finally, there has been a great proliferation of clubs and private individuals devoted to the rearing of horses for show, racing, and riding. The Nation's 4-H Horse Club projects now outnumber the 4-H beef projects. In 1974, there were 320,000 horse projects and 168,800 beef projects.

Intestinal parasites cause particularly heavy losses in young horses. It is estimated that the 2 million foals born annually are treated on an average of 4 times with anthelmintic drugs at a total cost of approximately $28 million. It is also estimated that the mortality in foals from helminths is 5 percent or 100,000 per year. At $500 per head, present mortality losses are $50 million. By the application of information expected to be derived from planned research, these losses can be appreciably reduced.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	1.1	$105,400	3.2
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		7

1.4 Equine Piroplasmosis (EP)

A Current Technology. The population of light horses in the U.S. in 1975 was estimated to number 9 million. These animals are used for recreation and racing. Their value for these activities makes it desirable to prevent EP from becoming the enzootic and chronic debilitating disease problem that it is in much of the world.

The 1966 return of taxes ($388 million) based on $4.5 billion of parimutuel betting has increased considerably with the institution of off-track betting in New York State. The combined parimutuel betting of over $500 million at Yonkers and Roosevelt Raceways has held about steady in recent years. Individual horse earnings of over $1 million have occurred. The quarantine of racing horses for the season or the closing of a track for a season could cost $100 million.

The causative agents (Babesia caballi and B. equi) are parasites of red blood cells that are transmitted from horse-to-horse by ticks. Progress has been made in the area of differential diagnosis of the two clinically indistinguishable infectious diseases of horses that primarily attack the circulatory system. The complement-fixation (CF) test developed by a USDA research team as an official diagnostic test for EP and the agar-gel immunodiffusion (AGID) test as an official diagnostic test for equine infectious anemia (EIA) provide reasonably satisfactory tools for preventing the interstate movement and importation of horses infected with these diseases. There are still problems in the area of antigen production for EP testing that need further study.

An experimental drug, Imidocarb dipropionate, [3,3'bis-(2-imidazolin-2 yl) carbanilide dipropionate] has been shown to be very effective against B. caballi, but relatively effective against B. equi. Residues in tissues may be a problem with this drug, so drug screening to find other drugs with fewer residue problems is needed.

Identification of vector ticks, particularly for B. equi, is still needed. The physiologic processes within the tick related to transmission of the disease and the necessary interactions between host, tick vectors, and parasites are unclear. Knowledge of other potential arthropod vectors is fragmentary. Tick control is accomplished by treatment of individual animals with ixodicidal preparations.

B Visualized Technology. Reduce losses due to equine piroplasmosis and facilitate freer movement of horses by: Improving antigens and production of antigens for use in a CF test and a card test for detecting infection with B. caballi or B. equi; studying intermediary metabolism of the parasites to detect attack points for drugs; studying interrelationships of equine Babesias with the hosts and tick vectors; using other Babesia species as model systems to lower the cost of research; determining details of the transmission cycle and physiologic relationships between vector(s) and parasites; determining alterations in the serologic response of horses following babesiacidal therapy; discovering new and better drugs for treatment of equine babesiosis.

C Research Approaches. The contemplated research requires a multidisciplinary approach. Immunology, veterinary medicine, biochemistry, entomology, pathology, and epizootiology all have their place. Research is directed toward:

Improvement of diagnostic antigens: What can be done to increase the proportion of successful passages in antigen production? What is the chemical nature of the antigen? What purification methods will improve the relatively crude antigens now in use? How can antigenic specificity best be preserved?

Study of known and potential tick vectors: Does feeding on unnatural hosts free the ticks of infection: What U.S. ticks are capable of transmitting B. equi? Is transmission of B. equi transovarial or transstadial? Does sexuality occur in Babesias, and how can it be studied and utilized most effectively?

Study of related Babesias: Is there any serologic relationship between Babesias found in wildlife and the equine Babesias? Can data acquired from small animal Babesias be predictive for situations involving large animal Babesias?

Study of pathogenesis of EP: What is the detailed pathology and histopathology of infection with B. equi?

Chemotherapy: What is the effect of drug treatment on the pathology of B. caballi and B. equi infections? What is the mechanism of action of drugs that affect the parasites? Can safer and more effective drugs be discovered?

D Consequences of Visualized Technology. Enable horses to move more freely interstate and internationally without increasing the danger of extending the enzootic area of these dangerous diseases; prevent deaths of valuable breeding and racing horses and allow racing horses to reach their full potential; provide knowledge and technology that can be used to keep the U.S. free of Babesias of other farm animals; provide knowledge and technology that may be useful in understanding protozoan diseases of man and aid in their control; provide knowledge and technology that will increase knowledge of ticks and their vector potential; conserve land resources and provide increased recreation.

E Potential Benefits. Because of the widely varying value of individual animals among the 9 million U.S. horses, their total value is almost impossible to estimate. By extrapolating 1970 figures, the current value of the horse industry can be estimated to be about $4.5 billion. A similar extrapolation gives a value of $7.5 billion volume of business annually for the buying and caring for horses. If present trends continue, an increase of 25 percent can be projected for 1980 and 50 percent for 1985. Any research efforts that lead to tools for preventing the importation and movement of horses infected with EP or for effectively curing such horses of their infections will protect these values.

At present, horses from Puerto Rico and other countries in the Caribbean area are practically excluded from importation into the U.S. because most of them are carriers of B. caballi, B. equi, or both. Identification of these animals and subsequent treatment would enable them to achieve their full potential as racing or show horses. The defining of enzootic foci would enable horse owners who follow racing and show circuits to avoid such areas and thus prevent their horses from being exposed to infected animals or tick vectors. Dangers from this disease are only potential in the U.S., except for southeastern Florida; however, large numbers of horses are shipped to enzootic areas around the world for shows and competitions and must be tested before reentering the U.S. to make sure they have not contracted the disease overseas. In some Florida herds, up to 80 percent of the animals have been infected, with a mortality of 10 percent. Most of the loss was in poor performance by sick animals and their potential for establishing new foci of disease during their travels.

Elimination of equine piroplasmosis from the U.S. would cause an estimated direct savings of $4.5 million annually related to death or infection of horses. Increased income due to ability to move horses more freely across state and national borders is incalculable. Additional losses would occur if race tracks had to be closed because of disease outbreaks.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	3.3	$240,300	4.3
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		8

Other Animals

1.1 Mink Diseases

A Current Technology. Distemper is presently regarded as the most important acute infectious disease of mink. The immune response of mink plays a major role in determining whether or not the host can eliminate the virus. It is apparent that both the antibody response (B cell) and cell-mediated immunity response (T cell) are important in the determination of the outcome of the disease. There is a question on how to actively immunize young mink that have maternal antibody. Colostral antibody suppression of active immunity in the young mink is a major problem.

Millions of mink are immunized by spray vaccination. Parenteral versus local immunization by spray vaccination is an important concept in vaccination programs. It would appear that vaccines administered locally on exposed epithelium are more advantageous than those given by the usual parenteral manner. The important point is that the understanding of the initial site of viral replication should be known and protective.

There is only one antigenic type of the distemper virus. First, the existence of different types is unlikely because one would expect that second attacks of the disease would be far more common, if there are more than one antigenic type. Secondly, differences in specificity have not been distinguished by cross-protection tests. Although all strains are antigenically the same, distemper virus can give rise to mutants of lower and higher virulence. The mechanisms of virulence with regard to the distemper virus are an enigma. Furthermore, some strains are highly neurotropic; some are not.

There is only fragmentary information concerning the stability of pathogenic distemper virus. Available knowledge contributes nothing to our understanding of airborne transmission. The crucial questions are: What is the stability of the virus in saliva and nasal exudate on fomites? What are the effects of temperature, humidity, sunlight, and air dilution on the virus in the form of large droplets, droplet nuclei, and dust? What is the relationship of aerosol droplet size and concentration to infection?

There is no really good information on the pathogenesis of demyelinating encephalomyelitis. Two possibilities present themselves. First, following viral replication, there is a direct effect on the virus on the neurons or oligo cells. Secondly, the encephalitis is a result of an immune immediated mechanism where antibody and complement and cellular immunity play a role. Additional data are needed to learn of the role of these various factors.

Hemorrhagic pneumonia caused by Pseudomonas aeruginosa is a devastating bacterial disease of ranch-raised mink. The losses may double each day until the disease has run its course on a mink farm. Vaccines are not available for the prevention of this disease. The only control measure currently available is the use of sulfathiazole. The treatment is not effective and recurrent losses continue for a considerable length of time. The epizootiology is not well understood. While the organism is present in the soil, feces, and standing water throughout the year, for some unknown reason, an outbreak of pneumonia ensues in which the organism is transmitted from mink-to-mink through the air.

The lesions are those of an acute hemorrhagic pneumonia with a marked necrotic component. Many strains of the agent are isolated on bacterial examination and the virulence and the sensitivity of these strains to antibiotics vary from among isolates. The infectious period is not known, and it is not known how long the mink may harbor the organism after recovery. The role of the carrier animal is unknown.

Since the late 1960's mink farmers in Utah and elsewhere have reported a "new" enteritis of mink. The clinical signs are similar to those of mink virus enteritis, but the mortality is low. The disease has a marked effect on the pelt. The reduction in pelt values has been a serious economic factor in mink production.

The disease is most likely to occur at stress periods during the mink raising cycle. September and October and on into pelting time in November are the months of highest incidence.

The malady presents a picture of the widespread infectious disease. About 100 farms have now reported outbreaks. The condition does not appear to be a nutritional disease. Recovered mink are immune to second attacks. Although this enteric disease appears similar to mink virus enteritis, it occurs in mink vaccinated against mink virus enteritis. There are no vaccines for the prevention of the new enteritis. The only treatments that can be recommended are those for bacterial enteritis.

B Visualized Technology. The objectives of the research program are: Establish means to overcome colostral antibody suppression of active immunity; determine the mechanism concerned in the production of encephalomyelitis, and study the stability of the agent under natural conditions; develop quick, accurate diagnostic methods to differentiate hemorrhagic pneumonia from other pneumonic conditions of mink; develop effective vaccines against known field isolates of P. aeruginosa; determine the factors influencing the outbreak.

Visualized technology is the establishment of effective control measures for this new enteritis through the development of vaccines. The development of an effective live virus vaccine is dependent upon the replication of the virus in a convenient laboratory system. This has not been accomplished.

C Research Approaches. Increase the amount of the antigen in the vaccine; alter the route of vaccine administration; use a heterotype virus for vaccination; study the mechanism of virulence by serial backpassage of the virus through ferrets; study the role of antibody (antiviral, antimyelin) or complement and cellular immunity in the production of distemper encephalitis; use cell culture procedures to isolate and quantitate the virus after exposure in natural situations.

Study the pathogenesis of the disease by exposing mink to known numbers of organisms by the airborne route. These mink will be killed sequentially. Tissues will be removed for bacterial examination, immunofluorescent studies, electron microscopy, and light microscopy. There may be an associated toxin, and toxin identification studies will also be conducted.

These studies will correlate agent virulence, clinical signs, gross and histological lesions, electron microscopy, and serological responses to infections.

Adapt the virus to a convenient laboratory system, such as cell culture (cell lines and primary cells) or the developing chicken embryo; prepare and test inactivated vaccines; prepare and test live virus vaccines; study the antigenic relationship of the new enteritis to mink virus enteritis; study and compare isolates obtained from different areas; develop convenient diagnostic tests.

D Consequences of Visualized Technology. Further understanding of the pathogenesis of distemper, since distemper has a slow component, may lead to control of certain virus infections of man, such as subacute sclerosing panencephalitis. The research should lead to more effective immunization and control procedures. An understanding of the disease processes would lead to better methods of disease control. Complete success in controlling hemorrhagic pneumonia might be possible with a vaccine. The only other species in which serious outbreaks of hemorrhagic pneumonia caused by Pseudomonas pneumonia occur is in hospital nurseries. Here, again, the bacteria use the airborne route. Many deaths of young infants have been recorded throughout the U.S. It is thought that the study of the disease of mink would also lead to the control of the disease in man.

The real potential benefit from the successful achievement of the technological objectives would be to lower the cost of producing mink. In addition, mink use about $150 million worth of agricultural by-products per year. These consist of fish scraps, poultry by-products, beef scraps, and some cereal grains. It is well known that mink patronage, in many instances, has meant the difference between profit and loss for industries having by-products for disposal.

The production of mink pelts in the U.S. is approximately 4,000,000, with an average selling price of $20 per pelt (total--$80,000,000 per year). Disease losses from all causes are estimated to be $5,000,000 per year.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	1.0	$82,000	3.0
SAES				
Others				
Total				
Years required for ARS to achieve the Visualized Technology		10		8

Because of the wide variety of disease conditions encountered in mink, such as bacterial, viral, nutritional, genetic, etc., it is recommended that 2 additional scientists be assigned to the Pioneering Research Laboratory to work on these disease problems. Without increased SY's on the problem, it will take many years to develop the technology outlined. An increase in animal holding and isolation facilities is needed to speed up the research work.

1.2 Rabbit Diseases

A Current Technology. There are 250,000 individuals involved in the rabbit industry. Many are low-income, backyard farmers. Some of the problems of the industry are due to poor management and may be solved by education of the grower, but intensive research to determine the cause, effective prevention and treatment, and mechanisms of resistance is required. Little basic information is available on the etiology, pathology, prevention, and treatment of rabbit diseases. A few diseases, such as pasteurellosis, coccidiosis, and myxomatosis are widely recognized, but others are poorly understood. Many rabbits are used in biomedical research. All experimental rabbit colonies have problems with infections from a wide variety of these agents. These potentially influence the outcome of experimentation.

B Visualized Technology. Study the types of diseases causing losses in domestic rabbits and develop information for the cause, prevention, and treatment of these diseases.

C Research Approaches. Additional research is needed to determine what etiologic agents are involved in gastrointestinal disorders, respiratory infection, infant mortality, and enzootic abortions? What histopathological and biochemical changes occur in tissues and body fluids, and what relationship does this have to the pathogenesis of disease? Do humoral and cellular mechanisms play a role in resistance? Are specific diagnostic tests possible? When an etiological agent is recovered, can a vaccine be developed? Can resistant strains of animals be developed? Can a specific-pathogen-free animal be developed for biomedical research?

D Consequences of Visualized Technology. Increase income of present growers. Permit more people to grow rabbits to provide either a primary or supplemental source of income. A combination of these two items will eventually lower the price to consumers. Development of an animal more suitable for laboratory experimentation and research. Glaucoma, malocclusion, and hydrocephalus in rabbits offer animal models for understanding comparable conditions in humans. Reduce farm and processing plant labor costs. Increase the use of agriculture by-products.

E Potential Benefits. The farm value of rabbit fryer production is estimated to be approximately $12 million. Biomedical research utilizes from 500,000 to 600,000 animals ($10 per rabbit = $6 million), yearly. Based on a fryer mortality of 35 percent and a 20 percent loss in research-raised rabbits, total loss due to mortality is estimated at $4.7 million, annually.

F Research Effort.

	Current Support			Expanded Support
	Year	SY's	Gross Dollars	SY's (ARS only)
ARS	1975	0	0	1
SAES				
Others				
Total				

Years required for ARS to achieve the Visualized Technology ____ ____

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V APPROVAL

Recommend	Edwin R. Goode Jr. — Responsible NPS Scientist	9/27/76 — Date
Concur	T. B. Kinney — Assistant Administrator	10/21/76 — Date
Concur	E. L. Corley — Director, PACS	10-26-76 — Date
Approval	Ralph J. McCracken — Associate Administrator	10/27/76 — Date

NOTE: The expanded support level reflected in this National Research Program represents Staffs' views as to the additional level of staffing that can be effectively used in meeting the long-term visualized objectives for this program. These do not reflect commitments on the part of the Agency.

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